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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/053,422	11/02/2001	Paul Polakis		7194

7590 05/02/2003

ONYX Pharmaceuticals, Inc.
3031 Research Drive
Richmond, CA 94806

EXAMINER	
CHEN, SHIN LIN	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 05/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
10/053,422	Polakis et al.
Examiner	**Art Unit**
Shin-Lin Chen	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Mar 25, 2003* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above, claim(s) *1-5 and 9-11* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *6-8* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's election without traverse of group IV, claims 6-8, in Paper No. 4 is acknowledged.

2. Claims 1-5 and 9-11 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 4.

Applicants' preliminary amendment filed 11-2-01 has been entered. Claims 1-11 are pending and claims 6-8 are under consideration.

It should be noted that the elected invention is drawn to a method of diagnosing for disease, such as cancer, by determining the presence of **beta-catenin protein**, and such is under examination by examiner.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 6-8 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MEP. § 2172.01. The omitted steps are: how to determine the presence of stabilized beta-catenin in a cell and whether the presence or absence of stabilized beta-catenin in a cell is indicative of the disease.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 6-8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 6-8 are directed to a method of diagnosing for disease based on unwanted cell growth, such as cancer or melanoma, comprising determining the presence of stabilized beta-catenin in said cells.

The specification discloses mutant beta-catenin protein having ser37phe or ser45tyr in various melanoma cell lines including 541 mel, 1241 mel, 624 mel, 888 mel and 1290 mel, and said mutant beta-catenin protein has longer protein half life as compared to wild type beta-catenin protein. The specification also discloses that wild type APC tumor suppressor down-regulates the amount of wild type beta-catenin protein in 928 mel and 1335 mel cell lines (specification, p. 10-12). The claims encompass diagnosing any disease having unwanted cell growth, any type of cancer and melanoma by determining the presence of wild type or mutant beta-catenin protein in any biological sample, such as blood, saliva, lymphoid fluid, any biopsy tissue sample etc., *in vitro* or *in vivo*.

The specification fails to provide adequate guidance and evidence for how to determine the presence of wild type or mutant beta-catenin protein *in vitro* or *in vivo*, and whether the presence of said beta-catenin protein is indicative of the presence of absence of any disease having unwanted cell growth, any cancer, or melanoma. Different diseases having unwanted cell growth, such as unwanted cell growth in blood vessel after angioplasty, and different types of cancers differ morphologically, physiologically, and pathologically. The mechanisms of how the unwanted cells grow and the gene(s) involved in various diseases having unwanted cell growth including cancers could vary from each other dramatically. Further, the type of biological sample used to determine the presence of wild type or mutant beta-catenin protein plays an important role in diagnosing the disease having unwanted cell growth. The specification fails to provide adequate guidance and evidence whether the wild type or mutant beta-catenin protein would be present in sufficient amount in the biological sample used, such as blood, saliva, or biopsy sample from various tissues, such that said beta-catenin protein can be detected for diagnosing the diseases having unwanted cell growth *in vitro* or *in vivo*. The specification also fails to provide adequate guidance for how to determine the presence of wild type or mutant beta-catenin protein *in vivo*, and one skilled in the art at the time of the invention would not know how to conduct the assay ***in vivo*** so as to diagnose any disease having unwanted cell growth in a patient.

The specification also fails to provide adequate guidance and evidence for the correlation between the presence or amount of wild type or mutant beta-catenin protein detected and the presence or absence of a particular disease having unwanted cell growth, such as a particular

cancer or melanoma. There is no evidence of record in the specification that the presence or any amount of wild type or mutant beta-catenin protein would be indicative of the presence or absence of a disease having unwanted cell growth, such as a particular type of cancer. Longer protein half life of mutant beta-catenin protein as compared to wild type beta-catenin protein or down-regulation of wild type beta-catenin by wild type APC tumor suppressor *in vitro* does not necessarily mean that presence or any amount of wild type or mutant beta-catenin protein in any biological sample would be indicative of the presence or absence of a disease having unwanted cell growth *in vitro* or *in vivo*. As discussed above, the mechanisms of how the unwanted cells grow and the gene(s) involved in various diseases having unwanted cell growth including cancers could vary from each other dramatically. Absent the correlation between the presence or amount of wild type or mutant beta-catenin protein detected and the presence or absence of a particular disease having unwanted cell growth, one skilled in the art at the time of the invention would not know how to diagnose a disease having unwanted cell growth via detection of either wild type or mutant beta-catenin protein *in vitro* or *in vivo*.

Therefore, it is concluded that based upon the nature of the claimed invention, the state of the art, the unpredictability found in the art, the teaching and working examples provided, and the breadth of the claims that it would require one skilled in the art at the time of the invention undue experimentation to practice over the full scope of the invention claimed.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (703) 305-1678. The examiner can normally be reached on Monday to Friday from 9 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds can be reached on (703) 305-4051. The fax phone number for this group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Shin-Lin Chen, Ph.D.